Patent claims

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1. A 6-carboxyphenyldihydropyridazinone derivative of the general formula

$$O = \begin{pmatrix} A & A & D \\ N-N & A & D \\ R^2 & G & E \end{pmatrix} C - R^3$$
 (I)

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in which

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A, D, E and G are identical or different and represent hydrogen, halogen, trifluoromethyl or hydroxyl, or represent (C₁-C₆)-alkyl or represent (C₁-C₆)-alkoxy,

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R¹ and R² are identical or different and represent hydrogen or represent (C₁-C₆)-alkyl,

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R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

group of the formula -NR⁷R⁸,

in which

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denotes cycloalkyl having from 3 to 8 carbon atoms or (C₁-C₈)-alkyl which is optionally substituted by hydroxyl, (C₁-C₆)-alkoxy, cycloalkyl having from 3 to 8 carbon atoms or aryl having from 6 to 10 carbon atoms which, for its part, can be substituted, once to twice, identically or differently, by substituents which are selected from the group: halogen, (C₁-C₆)-alkoxy, hydroxyl or trifluoromethyl, or denotes (C₁-C₈)-alkyl which is optionally substituted by a

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in which

 R^7 and R^8 are identical or different and denote hydrogen, (C₁-C₆)-alkyl or benzyl,

or

R⁴ denotes vinyl or allyl,

or

denotes aryl having from 6 to 10 carbon atoms which is optionally substituted once to twice, identically or differently, by substituents which are selected from the group consisting of: halogen, (C₁-C₆)-alkyl, (C₁-C₆)-alkoxy or hydroxyl,

R⁵ denotes hydrogen or (C₁-C₄)-alkyl,

R⁶ denotes cycloalkyl having from 3 to 8 carbon atoms or a radical of the formula

or

aryl having from 6 to 10 carbon atoms or a 5- to 7-membered aromatic heterocycle having up to 3 heteroatoms from the series S, N and/or O, it being possible for the ring systems which are listed here to be optionally substituted, once to several times, identically or differently, by substituents which are selected from the group: halogen, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, carboxyl, (C₁-C₆)-alkoxycarbonyl

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 (C_1-C_6) -alkyl and radicals of the formulae $-SO_2-NR^9R^{10}$ and $-(CO)_a-NR^{11}R^{12}$,

in which

R⁹, R¹⁰, R¹¹ and R¹² are identical or different and denote hydrogen or (C₁-C₆)-alkyl,

and

a denotes a number 0 or 1,

or

denotes (C₁-C₈)-alkyl which is optionally substituted, once to twice, identically or differently, by substituents which are selected from the group: halogen, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, carboxyl, (C₁-C₆)-alkoxycarbonyl and aryl having from 6 to 10 carbon atoms and a 5- to 7-membered aromatic heterocycles having up to 3 heteroatoms from the series S, N and/or O, in which the ring systems can be optionally substituted, once to three times, identically or differently, by (C₁-C₆)-alkyl, halogen, (C₁-C₆)-alkoxy, (C₁-C₆)-alkoxycarbonyl, trifluoromethyl or by the radical -CO-NH₂,

or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae

contd. a^1

which, for their part, can be optionally substituted,

5 and the salts thereof,

with the exception, however, of the compound N-methyl-4-(4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)benzamide.

10 2. A 6-carboxyphenyldihydropyridazinone derivative of the general formula (I) as claimed in claim 1,

in which

A, D, E and G are identical or different and represent hydrogen, fluorine, chlorine, bromine or trifluoromethyl,

R¹ and R² are identical or different and represent hydrogen or represent methyl,

R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

in which

denotes cyclopropyl, cyclopentyl or cyclohexyl or

denotes (C₁-C₆)-alkyl which is optionally substituted by
hydroxyl, (C₁-C₄)-alkoxy, cyclopropyl, cyclopentyl,

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cyclohexyl or phenyl which, for its part, can be substituted once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, bromine, (C₁-C₄)-alkoxy, hydroxyl or trifluoromethyl, or

denotes (C₁-C₆)-alkyl which is optionally substituted by a group of the formula -NR⁷R⁸,

in which

R⁷ and R⁸ are identical or different and denote hydrogen or (C₁-C₄)-alkyl,

or

R⁴ denotes allyl,

 R^5 denotes hydrogen or (C_1-C_3) -alkyl,

denotes cyclopropyl, cyclopentyl or cyclohexyl or denotes phenyl, thienyl, thiazolyl, furyl or pyridyl, it being possible for the listed aromatic ring systems to be optionally substituted, once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, bromine, trifluoromethyl, hydroxyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, (C₁-C₄)-alkyl and radicals of the formulae -SO₂NR⁹R¹⁰ and -(CO)_a-NR¹¹R¹²,

in which

 R^9 , R^{10} , R^{11} and R^{12} are identical or different and denote hydrogen or (C_1-C_4) -alkyl,

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Hants then that there is to

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and

a

or

denotes a number 0 or 1,

formula -CO-NH₂,

R⁶ denotes (C₁-C₆)-alkyl which are optionally substituted once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, bromine, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, (C₁-C₄)-alkoxycarbonyl, phenyl, pyridyl, naphthyl, furyl or thiazolyl, it being possible for the ring systems to be optionally substituted, once to twice, identically or differently, by fluorine, chlorine, methyl, methoxycarbonyl, trifluoromethyl or by a radical of the

or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae

and the salts thereof,

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with the exception, however, of the compound N-methyl-4-(4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)benzamide.

3. A 6-carboxyphenyldihydropyridazinone derivative of the general formula (I) as claimed in claim 1.

in which

A, D, E and G represent hydrogen,

 R^1 and R^2 are identical or different and represent hydrogen or represent methyl,

R³ represents radicals of the formulae -OR⁴ or/-NR⁵R⁶,

in which

denotes cyclopropyl, cyclopentyl or cyclohexyl or denotes (C₁-C₅)-alkyl which is optionally substituted by (C₁-C₄)-alkoxy, cyclopropyl, cyclopentyl, cyclohexyl or phenyl which, for its part, can be substituted, once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, (C₁-C₄)-alkoxy, hydroxyl or trifluoromethyl, or

denotes (C/C₄)-alkyl which is optionally substituted by a group of the formula -NR⁷R⁸,

in which

R⁷ and R⁸ are identical or different and denote hydrogen, benzyl or methyl,

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 R^4 \ denotes allyl,

 R^5 denotes hydrogen or (C_1-C_3) -alkyl,

denotes cyclopropyl, cyclopentyl or cyclohexyl or denotes naphthyl, phenyl, thienyl, thiazolyl, furyl or pyridyl, the listed ring systems being optionally substituted once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, bromine, trifluoromethyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, (C₁-C₃)-alkyl and radicals of the formulae -SO₂-NR⁹R¹⁰ and -(CO)_a-NR¹¹R¹²,

in which

R⁹, R¹⁰, R¹¹ and R¹² are identical or different and denote hydrogen or (C₁-C₄)-alkyl,

and

a denotes a number 0 or 1,

or

R⁶ denotes (C₁-C₆)-alkyl which is optionally substituted by substituents selected from the group: fluorine, chlorine, trifluoromethyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarconyl, phenyl, pyridyl, naphthyl, furyl, thienyl or thiazolyl, the ring systems optionally being substituted once to twice, identically

or differently, by fluorine, chlorine, methyl, methoxycarbonyl or trifluoromethyl or by a radical of the formula -CO-NH₂,

or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae

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and the salts thereof,

with the exception, however, of the compound N-methyl-4-(4-methyl-6-oxo-1,4,5,6-tetrahydropyridazin-3-yl)benzamide.

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A 6-carboxyphenyldihydropyridazinone derivative of the general formula (I) 4. as claimed in claim 1,

in which

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A, D, E and G represent hydrogen,

represents the radical -NR⁵R⁶, where $R^5 = H$ or methyl and R^6 is as R^3 previously defined,

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and the remaining radicals have the previously mentioned meaning

contd. a^1

- 5. A process for preparing 6-carboxy-phenyl-dihydropyridazinone derivatives as claimed in claims 1-to 4, characterized in that
 - [A] in the case where R³ represents the radical of the formula -OR⁴ in the above general formula (I),

compounds of the general formula (II)

$$CO_2H$$
 CO_2H
(II),

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in which

A, D, R¹ and R² have the abovementioned meaning,

are initially converted, by reaction with carboxylic acid-activating reagents, using customary methods, into the compounds of the general formula (IV)

$$R^1$$
 $N-N$
 R^2
 $CO-L$
(IV),

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in which

A, D, \mathbb{R}^1 and \mathbb{R}^2 have the abovementioned meaning,

and

represents an activating radical, preferably chlorine or imidazolyl,

and, in a second step, reacted with compounds of the general formula

(III),

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 R^4

in which

(III)

has the abovementioned meaning,

in inert solvents, where appropriate in the presence of a base,

HO-R⁴

or

in the case where \mathbb{R}^3 represents the radical of the formula $-\mathbb{N}\mathbb{R}^5\mathbb{R}^6$ in [B] the above general formula (I),

compounds of the general formula (II) are initially converted, by reaction with carboxylic acid-activating reagents, and using customary methods, into the compounds of the general formula (IV)

$$R^{1}$$
 $N-N$
 R^{2}
 (IV)

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in which

A, D, R¹ and R² have the abovementioned meaning,

- 46 -

and

represents an activating radical, preferably chlorine or imidazolyl, L

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and, in a second step, reacted with amides of the general formula (V)

HNR⁵R⁶

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in which

R⁵ and R⁶ have the abovementioned meaning,

in inert solvents

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A medicament or pharmaceutical composition which comprises at least one 6. compound as claimed in claims 1 to 4 and also one or more pharmaco-Sogically harmless auxiliary and carrier substances.

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A medicament or pharmaceutical composition as claimed in claim 6 for the prophylaxis and/or treatment of anemias.

- A medicament or pharmaceutical composition as claimed in claim 6 or 7 for 8. treating premature baby anemias, anemias associated with chronic renal 11 insufficiency, anemias following chemotherapy and anemias in HIV patients.
- A medicament or pharmaceutical composition as claimed in claim 6 for 9. 11 stimulating the erythropoiesis of individuals donating their own blood
- The use of 6-carboxyphenyldihydropyridazinone derivatives of the general 10. formula (I)

contd a²

$$O = \begin{pmatrix} A & D & C \\ R^2 & G & E \end{pmatrix}$$
 (I)

in which

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A, D, E and G are identical or different and represent hydrogen, halogen, trifluoromethyl or hydroxyl, or represent (C₁-C₆)-alkyl or represent (C₁-C₆)-alkoxy,

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R¹ and R² are identical or different and represent hydrogen or represent (C₁-C₆)-alkyl,

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R³ represents radicals of the formulae -OR⁴ or -NR⁵R⁶,

group of the formula -NR⁷R⁸,

in which

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denotes cycloalkyl having from 3 to 8 carbon atoms or (C_1-C_8) -alkyl which is optionally substituted by hydroxyl, (C_1-C_6) -alkoxy, cycloalkyl having from 3 to 8 carbon atoms or aryl having from 6 to 10 carbon atoms which, for its part, can be substituted, once to twice, identically or differently, by substituents which are selected from the group: halogen, (C_1-C_6) -alkoxy, hydroxyl or trifluoromethyl, or

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denotes (C₁-C₈)-alkyl which is optionally substituted by a

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in which

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 R^7 and R^8 are identical or different and denote hydrogen, (C₁-C₆)-alkyl or benzyl,

or

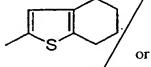
R⁴ denotes vinyl or allyl,

or

R⁴ denotes aryl having from 6 to 10 carbon atoms which is optionally substituted, once to twice, identically or differently, by substituents which are selected from the group consisting of: halogen, (C₁-C₆)-alkyl, (C₁-C₆) alkoxy or hydroxyl,

R⁵ denotes hydrogen or (C₁-C₄)-a/kyl,

R⁶ denotes cycloalkyl having from 3 to 8 carbon atoms or a radical of the formula



aryl having from 6 to 10 carbon atoms or a 5- to 7-membered aromatic heterocycle having up to 3 heteroatoms from the series S, N and/or O, it being possible for the ring systems which are listed here to be optionally substituted, once to several times, identically or differently, by substituents which are selected from the group: halogen, trifluoromethyl, hydroxyl, (C_1-C_6) -alkoxy, carboxyl, (C_1-C_6) -alkoxycarbonyl, (C_1-C_6) -alkyl and radicals of the formulae $-SO_2-NR^9R^{10}$ and $-(CO)_a-NR^{11}R^{12}$,

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which

 R^9 , R^{10} , R^{11} and R^{12} are identical or different and denote hydrogen of (C_1-C_6) -alkyl,

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and

a denotes a number 0 or 1,

or

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denotes (C₁-C₈)-alkyl which is optionally substituted, once to twice, identically or differently, by substituents which are selected from the group: halogen, trifluoromethyl, hydroxyl, (C₁-C₆)-alkoxy, carboxyl, (C₁-C₆)-alkoxycarbonyl and aryl having from 6 to 10 carbon atoms and a 5- to 7-membered aromatic heterocycle having up to 3 heteroatoms from the series S, N and/or O, in which the ring systems can be optionally substituted, once to three times, identically or differently, by (C₁-C₆)-alkyl, halogen, (C₁-C₆)-alkoxy, (C₁-C₆)-alkoxycarbonyl, trifluoromethyl or by the radical -CO-NH₂,

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or

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R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the

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which, for their part, can be optionally substituted,

5 and the salts thereof,

for preparing medicaments of pharmaceutical compositions for the prophylaxis and/or treatment of anemias.

10 11. The use of 6-carboxyphenyldihydropyridazinone derivatives of the general formula (I) as claimed in claim 10,

in which

A, D, E and G are identical or different and represent hydrogen, fluorine, chlorine, bromine or trifluoromethyl,

R¹ and R² are identical or different and represent hydrogen or represent methyl,

 R^3 represents radicals of the formulae $-OR^4$ or $-NR^5R^6$, in which

25 R^4 denotes cyclopropyl, cyclopentyl or cyclohexyl or denotes (C_1-C_6) -alkyl which is optionally substituted by hydroxyl, (C_1-C_4) -alkoxy, cyclopropyl, cyclopentyl

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or phenyl which, for its part, can be substituted once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, bromine, (C₁-C₄)-alkoxy, hydroxyl or trifluoromethyl, or

denotes (C₁-C₆)-alkyl which is optionally substituted by a group of the formula -NR⁷R⁸,

in which

R⁷ and R⁸ are identical or different and denote hydrogen or (C₁-C₄)-alkyl,

or

R⁴ denotes vinyl or allyl,

R⁵ denotes hydrogen or (C₁-C₃)-alkyl,

denotes cyclopropyl, cyclopentyl or cyclohexyl or denotes phenyl, thienyl, thiazolyl, furyl or pyridyl, it being possible for the listed aromatic ring systems to be optionally substituted, once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, bromine, trifluoromethyl, hydroxyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, (C₁-C₄)-alkyl and radicals of the formulae -SO₂NR⁹R¹⁰ and -(CO)_a-NR¹¹R¹²,

in which

 R^9 , R^{10} , R^{10} and R^{12} are identical or different and denote hydrogen or (C_1-C_4) -alkyl,

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and

a

or

denotes a number 0 or 1,

formula -CO-NH_Q,

denotes (C₁-C₆)-alkyl which are optionally substituted once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, bromine, trifluoromethyl, hydroxyl, (C₁-C₄)-alkoxy, (C₁-C₄)-alkoxycarbonyl, phenyl, pyridyl, naphthyl, furyl or thiazolyl, it being possible for the ring systems to be optionally substituted, once to twice, identically or differently, by fluorine, chlorine, methyl, methoxycarbonyl, trifluoromethyl or by a radical of the

or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae

which are in turn optionally substituted,

and the salts thereof,

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for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of anemias.

5 12. The use of 6-carboxyphenyldihydropyridazinone derivatives of the general formula (I) as claimed in claim-10,

in which

10 A, D, E and G represent hydrogen,

R¹ and R² are identical or different and represent hydrogen or represent methyl,

15 R^3 represents radicals of the formulae $-9R^4$ or $-NR^5R^6$,

in which

denotes cyclopropyl, cyclopentyl or cyclohexyl or denotes (C₁-C₅) alkyl which is optionally substituted by (C₁-C₄)-alkoxy, cyclopropyl, cyclopentyl, cyclohexyl or phenyl which, for its part, can be substituted, once to twice, identically or differently, by substituents selected from the group: fluorine, chlorine, (C₁-C₄)-alkoxy, hydroxyl or trifluoromethyl, or

denotes (C_1-C_4) -alkyl which is optionally substituted by a group of the formula -NR⁷R⁸,

30 jn which

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contd. a^2

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R⁷ and R⁸ are identical or different and denote hydrogen, benzyl or methyl,

or

R⁴ denotes allyl,

R⁵ denotes hydrogen or (C₁-C₃)-alkyl,

denotes cyclopropyl, cyclopentyl or cyclohexyl or denotes naphthyl, phenyl, thienyl, thiazolyl, furyl or pyridyl, the listed ring systems being optionally substituted once to twice, identically or differently, by substituents selected from the group: fluorine chlorine, bromine, trifluoromethyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, (C₁-C₃)-alkyl and radicals of the formulae -SO₂-NR⁹R¹⁰ and -(CO)_a-NR¹¹R¹²,

in which

 R^9 , R^{10} , R^{11} and R^{12} are identical or different and denote hydrogen or (C_1-C_4) -alkyl,

and

a denotes a number 0 or 1,

or

R⁶ denotes (C₁-C₆)-alkyl which is optionally substituted by substituents selected from the group: fluorine, chlorine, trifluoromethyl, (C₁-C₃)-alkoxy, (C₁-C₃)-alkoxycarbonyl, phenyl, pyridyl, naphthyl, furyl, thienyl or thiazolyl, the ring

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ring systems optionally being substituted once to twice, identically or differently, by fluorine, chlorine, methyl, methoxycarbonyl or trifluoromethyl or by a radical of the formula -CO-NH₂,

or

R⁵ and R⁶ form, together with the nitrogen atom, cyclic radicals of the formulae

which are in turn optionally substituted,

and the salts thereof,

for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or reatment of anemias.

20 13. The use of 6-carboxyphenyldihydropyridazinone derivatives of the general formula (I) as claimed in claim 10,

in which

25 A, D, E and G represent hydrogen,

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 R^3 represents the radical -NR⁵R⁶, where $R^5 = H$ or methyl and R^6 is as previously defined,

and the remaining radicals have the previously given meaning,

and the salts thereof,

for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of anemias

14. The use as claimed in one of claims 10 to 13 for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of premature baby anemias, anemias associated with chronic renal insufficiency, anemias following chemotherapy and anemias in HIV patients.

15. The use as claimed in one of claims 10 to 13 for preparing medicaments or pharmaceutical compositions for stimulating the erythropoiesis of individuals atonating their own blood.

- 20 16. The use of erythropoietin sensitizers for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of anemias.
 - 17. The use as claimed in claim 16 for preparing medicaments or pharmaceutical compositions for the prophylaxis and/or treatment of premature baby anemias, anemias associated with chronic renal insufficiency, anemias following chemotherapy and anemias in HIV patients.
 - 18. The use of erythropoietin sensitizers for preparing medicaments or pharmaceutical compositions for stimulating the erythropoiesis of individuals donating their own blood.

19. The use as claimed in one of claims 16 to 18, characterized in that the erythropoietin sensitizers are administered orally.